REMARKS

Applicants have cancelled Claims 29-31 without prejudice to, or disclaimer of, the subject matter contained therein. Applicants maintain that the cancellation of a claim makes no admission as to its patentability and reserve the right to pursue the subject matter of the cancelled claim in this or any other patent application.

Applicants have amended the Claims 27, 28, 32, and 33 to remove reference to the Figures. Claim 27 was amended to delete reference to extracellular domains and signal peptides, and to correct typographical errors. Applicants maintain that the amendments add no new matter and are fully supported by the specification as originally filed. For example, support for the amendments to Claim 27 can be found at page 44, line 29, through page 45, line 0 of the specification.

Claims 27, 28 and 32-34 are presented for examination. Applicants respond below to the specific rejections raised by the Examiner in the Office Action mailed May 24, 2004. For the reasons set forth below, Applicants respectfully traverse.

Rejections under 35 U.S.C. § 112, first paragraph – Written Description

The PTO has rejected Claims 27-34 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one of skill in the relevant art that the inventors had possession of the claimed invention at the time the application was filed.

Citing the written description guidelines, the PTO states that in an analysis of a genus/species situation, "Satisfactory disclosure of a 'representative number' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." Office Action at 2-3 (quoting Revised Guidelines for Written Description, Fed. Reg. December 21, 1999 Vol.64, No. 244). The PTO argues that the use of "hybridization" language causes the claims to include variants for which no written description is provided since there is no description of any other sequence besides SEQ ID NO: 7 which "hybridizes" to SEQ ID NO: 7. The PTO argues that there are no common elements or attributes of the sequence disclosed, and there are no structural limitations or requirements which provide guidance on the identification of sequences which would meet these functional limitations.

The PTO also argues that the claims encompass alternately spliced versions of the proteins, allelic variants including insertions and mutations, inactive precursor proteins which have a removable amino terminal end, and only specific amino acid sequences have been provided. The PTO states that no written description of alleles, of upstream or downstream regions containing additional sequence, or of alternative splice variants has been provided in the specification.

The PTO notes that while Example 9 of the [written description] guidelines reads stringent hybridization conditions as yielding less variation, in this case the variations are significant because there is no expectation that other sequences which hybridize to SEQ ID NO: 7 would themselves hybridize to targets which are overexpressed in cancer cells, which the PTO states is the asserted utility of SEQ ID NO: 7.

The PTO asserts that while variants of SEQ ID NO: 7 are likely to exist, except for SEQ ID NO: 7, there is a complete absence of knowledge as to what sequence comprises these variants. Citing *Regents of University of California v. Eli Lilly and Co.*, 34 USPQ2d 1398 (Fed Cir. 1997), the PTO states that this is a situation of naming a type of material which is generally known to likely exist, but, except for SEQ ID NO: 7 itself, in the absence of knowledge of the material composition, fails to provide descriptive support for the generic claim to anything which hybridizes to SEQ ID NO: 7 under stringent conditions.

Finally, the PTO states that there is no conception of sequences which hybridize to SEQ ID NO: 7 except by the functional utility of "hybridization," and that Applicant has no definition of the structure of these molecules or of any structural element relating to these molecules whatsoever. The PTO concludes that the entire claim is functionally drawn to claim compounds which Applicant does not have, which Applicant has not made, and which comprise specific sequences Applicant does not know.

Applicants respectfully disagree, and will address each argument raised by the PTO.

The Legal Standard for Written Description

The well-established test for sufficiency of support under the written description requirement of 35 U.S.C. §112 , first paragraph is whether the disclosure "reasonably conveys to artisan that the inventor had possession at that time of the later claimed subject matter." *In re Kaslow*, 707 F.2d 1366, 1375, 2121 USPQ 1089, 1096 (Fed. Cir. 1983); see also *Vas-Cath, Inc.*

v. Mahurkar, 935 F.2d at1563, 19 USPQ2d at 1116 (Fed. Cir. 1991). The adequacy of written description support is a factual issue and is to be determined on a case-by-case basis. See e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116 (Fed. Cir. 1991). The factual determination in a written description analysis depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure. *Union Oil v. Atlantic Richfield Co.*, 208 F.3d 989, 996 (Fed. Cir. 2000).

The Current Invention is Adequately Described

Applicants initially note the claims are directed in part to nucleic acid molecules that hybridize under specified highly stringent conditions to a complement of a nucleic acid which encodes the *polypeptide* of SEQ ID NO: 7. Applicants assume that the PTO's reference to nucleic acids which hybridize to SEQ ID NO: 7, or nucleic acids of SEQ ID NO: 7, are simple oversight. SEQ ID NO: 6 is one example of a sequence which encodes the polypeptide of SEQ ID NO: 7. One of skill in the art would know how to make other nucleic acid sequences which encode the polypeptide of SEQ ID NO: 7 based on codon degeneracy. Thus, given that Applicants have disclosed SEQ ID NO: 7, what constitutes a complement of a nucleic acid sequence which encodes the polypeptide of SEQ ID NO: 7 would be understood by one of skill in the art.

Applicants next address the PTO's assertions that the use of hybridization language leads to variants for which no written description exists. Applicants submit that the limitation that the claimed nucleotides hybridize under specified highly stringent conditions is not a functional limitation as the PTO has characterized it, but rather is a structural limitation. As Examples 9 and 10 of the Application of Written Description Guidelines (hereinafter Guidelines) make clear, specifying hybridization under highly stringent conditions yields "*structurally* similar DNAs." (Guidelines, Example 9 at page 36) (emphasis added). The analysis of a genus claim in Example 10 of the Guidelines states:

> [T]urning to the genus analysis, the art indicates that *there is no substantial variation within the [claimed] genus because of the stringency of hybridization conditions which yields structurally similar molecules.* The single disclosed species is representative of the genus because reduction to practice of this species, considered along with the defined hybridization conditions and the level of skill and knowledge in the art, are sufficient to allow the skilled artisan to recognize that applicant was in possession of the necessary common attributes or features of

> the elements possessed by the members of the genus. (Guidelines, Example 10 at page 39) (emphasis added).

Thus, the PTO's own guidelines on written description view a hybridization limitation as a structural limitation. Given the level of skill in the art, specifying highly stringent conditions leads to "no substantial variation within the [claimed] genus," and therefore a skilled artisan would recognize that the applicant was in possession of the necessary common attributes or features of the genus. This directly contradicts the PTO's argument that no common element or attributes of the claimed sequences are disclosed. The common element or attribute of the claimed genus is that species of the genus are structurally related to SEQ ID NO: 6 or nucleic acid sequences which encode polypeptides of SEQ ID NO: 7, such that they hybridize to them under the specified highly stringent conditions.

The PTO acknowledges that this argument is supported by Example 9 of the Guidelines, but argues that variations allowed by the hybridization language are significant in the instant case because there is no expectation that other sequences which hybridize to SEQ ID NO: 7 would themselves hybridize to targets which are overexpressed in cancer cells, the asserted utility of SEQ ID NO: 7. Applicants submit that this argument in no way supports the PTO's prima facie case that Applicants have failed to satisfy the written description requirement. In this case, the intended use of the claimed nucleic acids has no bearing on whether they are adequately described by specifying high stringency conditions and the sequence to which they must hybridize. Applicants submit that the Guidelines teach that specific high stringency conditions and a known sequence are sufficient to describe a genus to those of skill in the art.

Likewise, the PTO's assertion that Applicants have named a material known to likely exist without any knowledge of what that material is, cannot stand in light of the teachings of the Guidelines. By knowing the target sequence and the specific stringent conditions under which the hybridization occurs, one of skill in the art would know what the claimed material is. This is unlike the facts in *Regents of the University of California v. Eli Lilly*, 43 USPQ2d 1398 (Fed. Cir. 1997), where the gene was defined not by its structure, i.e. sequence, but rather by what it did. Here, the claimed genus is defined by its structure – members of the genus hybridize under the specified conditions to the specified sequences. As discussed above, this is a structural limitation, not a functional limitation.

The instant case is also different from *Fiers v. Sugano*, 25 USPQ2d 1601, in that the gene in the instant case *has* been reduced to practice – the gene of SEQ ID NO: 6 has been cloned and sequenced. As the Guidelines indicate, no more than a single sequence and the specific high stringency conditions are required to support a genus claim. Given these two pieces of information, one of skill in the art would have all the description necessary to "recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus".

Finally, Applicants address the PTO's argument that the claims encompass alternately spliced versions of the proteins, allelic variants including insertions and mutations, inactive precursor proteins which have a removable amino terminal end, and that only specific amino acid sequences have been provided. The pending claims are directed to isolated nucleic acids which hybridize under the specified conditions to a complement of a nucleic acid sequence encoding the polypeptide of SEQ ID NO:7; the complement of a nucleic acid sequence of SEQ ID NO:6; a complement of the full-length coding sequence of the nucleic acid sequence of SEQ ID NO:6; or a complement of the full-length coding sequence of the cDNA deposited under ATCC accession number 203661. Each of the target sequences are adequately described in the specification. Applicants submit that the pending claims relate to nucleic acids which hybridize to the nucleic acids listed in the claims, not alternately spliced versions of the proteins, allelic variants including insertions and mutations, or inactive precursor proteins which have a removable amino terminal end.

In conclusion, Applicants submit that Applicants have satisfied the written description requirement by reducing the nucleic acid of SEQ ID NO: 6 to practice, and by specifying the high stringency conditions under which hybridization occurs. Together, this disclosure would allow one of skill in the art to "recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus." Thus, Applicants respectfully request that the PTO reconsider and withdraw its rejection of the pending claims under 35 U.S.C. § 112, first paragraph.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance. Nevertheless, the PTO is invited to contact the undersigned at the telephone number appearing below to discuss any remaining issues.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: August 20, 2004

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